

190 Claims

1. A compound of formula (I)

$$R^2$$
 R^1
 R^5
 R^4
 R^3
 R^4

or a salt, ester, amide or prodrug thereof;

where X is O, or S, S(O), S(O)₂ or NR⁶ where R⁶ is hydrogen or C_{1-6} alkyl; R⁵ is an optionally substituted 6-membered aromatic ring containing at least one nitrogen atom, and

 R^1 , R^2 , R^3 , R^4 are independently selected from halogeno, cyano, nitro, $C_{1\text{-}3}$ alkylsulphanyl, $-N(OH)R^7$ - (wherein R^7 is hydrogen, or $C_{1\text{-}3}$ alkyl), or R^9X^1 - (wherein X^1 represents a direct bond, -O-, $-CH_2$ -, -OC(O)-, -C(O)-, -S-, -SO-, $-SO_2$ -, $-NR^{10}C(O)$ -, $-C(O)NR^{11}$ -, $-SO_2NR^{12}$ -, $-NR^{13}SO_2$ - or $-NR^{14}$ - (wherein R^{10} , R^{11} , R^{12} , R^{13} and R^{14} each independently represents hydrogen, $C_{1\text{-}3}$ alkyl or $C_{1\text{-}3}$ alkoxy $C_{2\text{-}3}$ alkyl)), and R^9 is hydrogen, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy; provided that at least one of R^2 or R^3 is other than hydrogen.

2. A compound according to claim 1 wherein at least one group R¹, R², R³, R⁴ is a group R⁹X¹- and R⁹ is hydrogen, an optionally substituted hydrocarbyl group selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or cycloalkynyl, or combinations thereof; or an optionally substituted heterocyclyl group of from 4 to 20 ring atoms, at least one of which is a heteroatom such as oxygen, sulphur or nitrogen and where the optional substituents comprise at least one functional group selected from nitro, cyano, halo, oxo, =CR⁷⁸R⁷⁹, C(O)_xR⁷⁷, OR⁷⁷, S(O)_yR⁷⁷, NR⁷⁸R⁷⁹, C(O)NR⁷⁸R⁷⁹, OC(O)NR⁷⁸R⁷⁹, =NOR⁷⁷, -NR⁷⁷CONR⁷⁸R⁷⁹, -N=CR⁷⁸R⁷⁹, S(O)_yNR⁷⁸R⁷⁹ or

- -NR⁷⁷S(O)_yR⁷⁸ where R⁷⁷, R⁷⁸ and R⁷⁹ are independently selected from hydrogen, optionally substituted hydrocarbyl, optionally substituted hetercyclyl or optionally substituted alkoxy, or R⁷⁸ and R⁷⁹ together form an optionally substituted ring which optionally contains further heteroatoms such as oxygen, nitrogen, S, S(O) or S(O)₂, where x is an integer of 1 or 2, y is 0 or an integer of 1-3.
- 3. A compound according to claim 2 where hydrocarbyl, heterocyclyl or alkoxy groups R⁷⁷, R⁷⁸ and R⁷⁹ as well as rings formed by R⁷⁸ and R⁷⁹ are optionally substituted by halo, perhaloalkyl, mercapto, alkylthio, hydroxy, carboxy, alkoxy, heteroaryl, heteroaryloxy, cycloalkyl, cycloalkenyl, cycloalkynyl, alkenyloxy, alkynyloxy, alkoxyalkoxy, aryloxy (where the aryl group may be substituted by halo, nitro, or hydroxy), cyano, nitro, amino, mono- or di-alkyl amino, oximino or S(O)_yR⁹⁰ where y is as defined in claim 2 and R⁹⁰ is a alkyl.
- 4. A compound according to any one of the preceding claims wherein at least one group R¹, R², R³, R⁴ is a group R⁹X¹- and R⁹ is hydrogen or an alkyl group, optionally substituted with one or more groups selected from functional groups as defined in claim 2 or claim 3, or alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, cycloalkenyl or cycloalkynyl, any of which may be substituted with a functional group as defined in claim 2 or claim 3, and where any aryl, heterocyclyl, cycloalkyl, cycloalkenyl, cycloalkynyl groups may also be optionally substituted with hydrocarbyl such as alkyl, alkenyl or alkynyl.
- 5. A compound according to claim 1 wherein at least one group R¹, R², R³, R⁴ is a group R⁹X¹- and R⁹ is selected from one of the following twenty-two groups:

 hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, oxiranyl, fluoro, chloro, bromo and amino (including C₁₋₃alkyl and trifluoromethyl);
 -R^aX²C(O)R¹⁵ (wherein X² represents -O- or -NR¹⁶- (in which R¹⁶ represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R¹⁵ represents
 C₁₋₃alkyl, -NR¹⁷R¹⁸ or -OR¹⁹ (wherein R¹⁷, R¹⁸ and R¹⁹ which may be the same

or different each represents hydrogen, C_{1-5} alkyl. hydroxy C_{1-5} alkylor C_{1-3} alkoxy C_{2-3} alkyl));

3) $-R^bX^3R^{20}$ (wherein X^3 represents -O-, C(O) -S-, -SO-, -SO₂-, -OC(O)-, -NR²¹C(O)_s-,

 $-C(O)NR^{22}$ -, $-SO_2NR^{23}$ -, $-NR^{24}SO_2$ - or $-NR^{25}$ - (wherein R^{21} , R^{22} , R^{23} , R^{24} and R²⁵ each independently represents hydrogen, C₁₋₃alkyl, hydroxy C₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl and s is 1 or 2) and R²⁰ represents hydrogen, C₁₋₆alkyl, C₂₋ 6alkenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₆alkyl group may bear 1, 2 or 3 substituents selected from oxo, hydroxy, halogeno, cyclopropyl, amino, C1-alkylamino, C1-alkanoyldi-C1-alkylamino, C1-alkylthio, C1-alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C₁₋₄cyanoalkyl, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkylsulphonylC₁₋₄alkyl, C₁₋₄alkoxycarbonyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkylaminoC₁₋₄alkyl, di(C₁₋₄alkyl)aminoC₁₋₄alkyl, C₁₋₄alkylaminoC₁₋₄alkoxy. di(C₁₋₄alkyl)aminoC₁₋₄alkoxy and a group -(-O-)_f(R^{b'})_gD (wherein f is 0 or 1, g is 0 or 1 and D is a C₃₋₆cycloalkyl group or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from C₁₋₄alkyl)); 4) -R°X⁴R° X⁵R²⁶ (wherein X⁴ and X⁵ which may be the same or different are each -O-, C(O), -S-, -SO-, -SO₂-, -NR²⁷C(O)_s-, -C(O)_xNR²⁸-, -SO₂NR²⁹-, -NR³⁰SO₂- or -NR³¹- (wherein R²⁷, R²⁸, R²⁹, R³⁰ and R³¹ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl and s is 1 or 2) and R²⁶ represents hydrogen, C₁₋₃alkyl,hydroxyC₁₋₃alkylorC₁₋₃alkoxyC₂₋₃alkyl); 5) R³² (wherein R³² is a 4-6-membered cycloalkyl or saturated heterocyclic ring (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which cycloalkyl or heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C1-4alkyl, hydroxyC₁₋₄alkyl, cyanoC₁₋₄alkyl, cyclopropyl, C₁₋₄alkylsulphonylC₁₋₄alkyl,

C₁₋₄alkoxycarbonyl, carboxamido, C₁₋₄aminoalkyl, C₁₋₄alkylamino.

di(C₁₋₄alkyl)amino, C₁₋₄alkylaminoC₁₋₄alkyl, C₁₋₄alkylaminoC₁₋₄alkoxy, di(C₁₋₄alkyl)aminoC₁₋₄alkoxy nitro, amino, C₁₋₄alkoxy, C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, -C(O)NR³⁸R³⁹, -NR⁴⁰C(O)R⁴¹ (wherein R³⁸, R³⁹, R⁴⁰ and R⁴¹, which may be the same or different, each represents hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and a group -(-O-)f(C₁₋₄alkyl)gringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from C₃₋₆cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl);

- 6) -R^dR³² (wherein R³² is as defined hereinbefore);
- 7) ReR32 (wherein R32 is as defined hereinbefore);
- 8) -Rf R32 (wherein R32 is as defined hereinbefore);
- 9) R³³ (wherein R³³ represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with
- 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents selected from hydroxy, nitro, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, oxo, cyanoC₁₋₄alkyl, cyclopropyl,

C. alkylsulphonylC. alkyl C. alkovycarbonyl di(C. alkyl)amino

 C_{1-4} alkylsulphonyl C_{1-4} alkyl, C_{1-4} alkoxycarbonyl, di $(C_{1-4}$ alkyl)amino,

 C_{1} -alkylamino C_{1} -alkyl, C_{1} -alkanoyl, di(C_{1} -alkyl)amino C_{1} -alkyl,

 C_{1-4} alkylamino C_{1-4} alkoxy, di(C_{1-4} alkyl)amino C_{1-4} alkoxy, carboxy, carboxamido, trifluoromethyl, cyano, $-C(O)NR^{38}R^{39}$, $-NR^{40}C(O)R^{41}$ (wherein R^{38} , R^{39} , R^{40} and R^{41} , which may be the same or different, each represents hydrogen, C_{1-4} alkyl, hydroxy C_{1-4} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and a group $-(-O_{-1}(C_{1-4}$ alkyl)gringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from C_{3-6} cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic

- with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl);
- 10) -R^gR³³ (wherein R³³ is as defined hereinbefore);
- 11) -RhR33 (wherein R33 is as defined hereinbefore);
- 12) -Ri R33 (wherein R33 is as defined hereinbefore);

13) $-R^j X^6 R^{33}$ (wherein X^6 represents -O-, _C(O)-, -S-, -SO-, -SO₂-, -OC(O)-, -NR³⁸C(O)-, -C(O)NR³⁹-, -SO₂NR⁴⁰-, -NR⁴¹SO₂- or -NR⁴²- (wherein R³⁸, R³⁹, R⁴⁰, R⁴¹ and R⁴² each independently represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³³ is as defined hereinbefore); 14) $-R^k X^7 R^{33}$ (wherein X^7 represents -O-, C(O), -S-, -SO-, -SO₂-, -NR⁴³C(O)-, -C(O)NR⁴⁴-, -SO₂NR⁴⁵-, -NR⁴⁶SO₂- or -NR⁴⁷- (wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ and R⁴⁷ each independently represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³³ is as defined hereinbefore);

- 15) -R^mX⁸R³³ (wherein X⁸ represents -O-, -C(O)-, -S-, -SO-, -SO₂-, -NR⁴⁸C(O)-, -C(O)NR⁴⁹-, -SO₂NR⁵⁰-, -NR⁵¹SO₂- or -NR⁵²- (wherein R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹ and R⁵² each independently represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³³ is as defined hereinbefore);
- 16) -Rⁿ X⁹Rⁿ R³³ (wherein X⁹ represents -O-, -C(O)-, -S-, -SO-, -SO₂-, -NR⁵³C(O)-, -C(O)NR⁵⁴-, -SO₂NR⁵⁵-, -NR⁵⁶SO₂- or -NR⁵⁷- (wherein R⁵³, R⁵⁴, R⁵⁵, R⁵⁶ and R⁵⁷ each independently represents hydrogen, C₁₋₃alkyl, hydroxyC₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R³³ is as defined hereinbefore); 17) -R^p X⁹-R^{p1}IR³² (wherein X⁹ and R³² are as defined hereinbefore):
- 18) C_{2-5} alkenyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C_{1-4} alkylamino, N_{N-1} di(C_{1-4} alkylamino, aminosulphonyl, N_{N-1} di(C_{1-4} alkylaminosulphonyl;
- 19) C_{2-5} alkynyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, amino, C_{1-4} alkylamino, $\underline{N},\underline{N}$ -di(C_{1-4} alkyl)amino, aminosulphonyl, \underline{N} - C_{1-4} alkylaminosulphonyl and $\underline{N},\underline{N}$ -di(C_{1-4} alkyl)aminosulphonyl;
- 20) -R^tX⁹R^t'R³² (wherein X⁹ and R³² are as defined hereinbefore);
- 21) -R" X9 R" R32 (wherein X9 and R32 are as defined hereinbefore); and
- 22) $R^{v} R^{58}(R^{v'})_{q}(X^{9})_{r}R^{59}$ (wherein X^{9} is as defined hereinbefore, q is 0 or 1, r is 0 or 1, and R^{58} is a C_{1-3} alkylene group or a cyclic group selected from cyclopropyl, cyclobutyl, cyclopentylene, cyclohexylene or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3} alkylene group may bear 1 or 2 substituents selected from oxo,

hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano,

C₁₋₄cyanoalkyl, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl, C₁-alkylsulphonylC₁-alkyl, C₁-alkoxycarbonyl, C₁-aminoalkyl, C₁-alkylamino, di(C₁4alkyl)amino, C₁4alkylaminoC₁4alkyl, di(C₁4alkyl)aminoC₁4alkyl, C₁₋₄alkylaminoC₁₋₄alkoxy, di(C₁₋₄alkyl)aminoC₁₋₄alkoxy and a group--(-O-)f(C1-4alkyl)gringD (wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from C₃₋₆cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl); and R⁵⁹ is hydrogen, C₁₋₃alkyl, or a cyclic group selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, cyano, C₁₋₄cyanoalkyl, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkylsulphonylC₁₋₄alkyl, C₁₋₄alkoxycarbonyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkylaminoC₁₋₄alkyl, di(C₁₋₄alkyl)aminoC₁₋₄alkyl, C₁₋₄alkylaminoC₁₋₄alkoxy, di(C₁₋₄alkyl)aminoC₁₋₄alkoxy and a group -(-O-)_f(C₁₋₄alkyl)_gringD (wherein f is 0 or 1, g is 0 or 1 and D is a cyclic group selected from C₃₋₆cycloalkyl, aryl or 5-6-membered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halo and C₁₋₄alkyl);

and wherein Ra, Rb, Rb', Rc, Rc', Rd, Rg, Rj, Rn, Rn' Rp, Rp', Rt', Ru', Rv and Rv' are independently selected from C₁₋₈alkylene groups optionally substitued by one or more substituents selected from hydroxy, halogeno, amino,

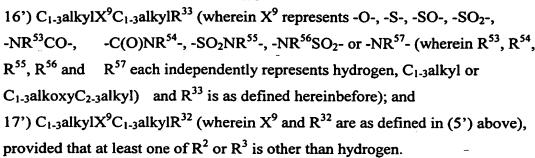
R^e R^h, R^k and R^t are independently selected from C₂₋₈alkenylene groups optionally substituted by by one or more substituents selected from hydroxy, halogeno, amino, and R' may additionally be a bond; and

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R^f, Rⁱ, R^m and R^u are independently selected from by C₂₋₈alkynylene groups optionally susbstituted by one or more substituents selected from hydroxy, halogeno, amino.

- 6. A compound according to claim 5 wherein R¹, R², R³, R⁴ are independently selected from, halo, cyano, nitro, trifluoromethyl, C₁₋₃alkyl, -NR⁷R⁸ (wherein R⁷ and R⁸, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or other groups from formula-X¹R⁹ (wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR¹⁰CO-, -CONR¹¹-, -SO₂NR¹²-, -NR¹³SO₂- or -NR¹⁴- (wherein R¹⁰, R¹¹, R¹², R¹³ and R¹⁴ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl), and R⁹ is selected from one of the following groups:
 - 1') hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro or amino, 2') C₁₋₅alkylX²C(O)R¹⁵ (wherein X² represents -O- or -NR¹⁶- (in which R¹⁵ represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R⁵ represents C₁₋₃alkyl, -NR¹⁷R¹⁸ or -OR¹⁹ (wherein R¹⁷, R¹⁸ and R¹⁹ which may be the same or different each represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl)); 3') C₁₋₅alkylX³R²⁰ (wherein X³ represents -O-, -S-, -SO-, -SO₂-, -OCO-, -NR²¹CO-, -CONR²²-, -SO₂NR²³-, -NR²⁴SO₂- or -NR²⁵- (wherein R²¹, R²², R²³, R²⁴ and R²⁵ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁰ represents hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl and C₁₋₄alkoxy);
 - 4') C_{1-5} alkyl X^4C_{1-5} alkyl X^5R^{26} (wherein X^4 and X^5 which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR²⁷CO-, -CONR²⁸-, -SO₂NR²⁹-, -NR³⁰SO₂- or -NR³¹- (wherein R²⁷, R²⁸, R²⁹, R³⁰ and R³¹ each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{26} represents hydrogen or C_{1-3} alkyl);

- 5') R³² (wherein R³² is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl and C₁₋₄alkylsulphonylC₁₋₄alkyl);
- 6') C₁₋₅alkylR³² (wherein R³² is as defined in (5') above);
- 7') C₂₋₅alkenylR³² (wherein R³² is as defined in (5') above);
- 8') C₂₋₅alkynylR³² (wherein R³² is as defined in (5') above);
- 9°) R³³ (wherein R³³ represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, cyano, -CONR³⁴R³⁵ and -NR³⁶COR³⁷ (wherein R³⁴, R³⁵, R³⁶ and R³⁷, which may be the same or different, each represents hydrogen, C₁₋₄alkyl or
- C_{1-3} alkoxy C_{2-3} alkyl));
- 10') C_{1-5} alkyl R^{33} (wherein R^{33} is as defined in (9') above);
- 11') C₂₋₅alkenylR³³ (wherein R³³ is as defined in (9') above);
- 12') C2-5alkynylR33 (wherein R33 is as defined in (9') above);
- 13') C_{1-5} alkyl X^6R^{33} (wherein X^6 represents -O-, -S-, -SO-, -SO₂-, -NR³⁸CO-, -CONR³⁹-, -SO₂NR⁴⁰-, -NR⁴¹SO₂- or -NR⁴²- (wherein R³⁸, R³⁹, R⁴⁰, R⁴¹ and R⁴² each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R³³ is as defined hereinbefore);
- 14') C_{2-5} alkenyl X^7R^{33} (wherein X^7 represents -O-, -S-, -SO-, -SO₂-, -NR⁴³CO-, -CONR⁴⁴-, -SO₂NR⁴⁵-, -NR⁴⁶SO₂- or -NR⁴⁷- (wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ and R⁴⁷ each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R^{33} is as defined hereinbefore);
- 15') C_{2-5} alkynyl X^8R^{33} (wherein X^8 represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁸CO-, -C(O)NR⁴⁹-, -SO₂NR⁵⁰-, -NR⁵¹SO₂- or -NR⁵²- (wherein R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹ and R⁵² each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl) and R³³ is as defined hereinbefore);



- 7. A compound according to any one of the preceding claims where R^1 is hydrogen and R^4 is hydrogen, halo, C_{1-4} alkyl or C_{1-4} alkoxy.
- 8. A compound according to any one of the preceding claims wherein at least one group R² or R³ comprises a chain of at least 3 optionally substituted carbon atoms or heteroatoms selected from oxygen, nitrogen or sulphur.
- A compound according to claim 8 wherein said chain is substituted by a polar group which assists solubility.
- 10. A compound according to any one of the preceding claims wherein R^3 is a group X^1R^9 where X^1 is oxygen and R^9 includes a methylene group directly adjacent X^1 .
- 11. A compound according to claim 5 wherein at least one of R¹, R², R³ or R⁴ is a group X¹R⁹ which includes a bridging alkylene, alkenylene or alkynylene groups R^a, R^b, R^b, R^c, R^c, R^d, R^g, R^j, Rⁿ, Rⁿ, R^p, R^p, R^t, R^t, R^v, R^v, R^v, R^e R^h, R^k R^t, R^f, Rⁱ, R^m and R^u and least one such group includes a hydroxy substituent.
- 12. A compound according to claim 5 wherein R⁹ is selected from a group of formula (1), (3), (6) or (10).
- 13. A compound according to any one of the preceding claims wherein X is NH orO.

- 14. A compound according to any one of the preceding claims wherein R⁵ is optionally substituted pyridine.
- 15. A compound according to any one of claims 1 to 13 where R⁵ is optionally substituted pyrimidine.
- 16. A compound according to claim 14 wherein R⁵ is a group of sub-formulae (i) or (ii)

where R^{80} is a large substituent of a chain of at least 4 atoms, and R^{81} is hydrogen halo, C_{1-4} alkoxy, cyano or trifluoromethyl, or phenyl.

17. A compound according to claim 15 where R⁵ is a group of sub-formula (iii), (iv) or (v)

where R⁸⁰ is a large substituent of a chain of at least 4 atoms, and R⁸¹ is hydrogen halo, C₁₋₄alkoxy, cyano or trifluoromethyl, or phenyl.

- 18. A compound according to claim 17 wherein R⁵ is a group of formula (iii).
- 19. A compound according to any one of claims 14 to 18 where pyridine or pyrimidine groups R⁵ are substitued by one or more groups selected from a) a functional group as defined in claim 2 or claim 3;

b) a hydrocarbyl selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or cycloalkynyl, or combinations thereof; any of which are optionally substituted by one or more functional groups as defined in claim 2 or claim 3;

- c) a heterocyclyl group optionally substituted by one or more functional groups as defined in claim 2 or claim 3 or hydrocarbyl groups selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or cycloalkynyl, or combinations thereof, wherein the hydrocarbyl group may be substituted by a functional group as defined in claim 2 or claim 3 or a heterocyclic group; d)alkoxy optionally substituted by a functional group as defined in claim 2 or claim 3, or a heterocylic group which is optionally substituted by a functional group as defined in claim 2 or claim 3.
- 20. A compound according to any one of the preceding claims wherein R⁵ is substituted by one or more groups selected from:
 - 1) halo, C₁₋₄alkyl, optionally substituted C₁₋₆ alkoxy, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, carboxy, benzoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C_{1-4} alkylsulphanyl, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, \underline{N} - C_{1} -alkylaminosulphonyl, \underline{N} , \underline{N} -di(C_{1} -alkyl)aminosulphonyl, C₁-alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2

substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl; 2) a group of sub-formula (II)

$$(CH_2)_{s'}$$
 X^{12} $(CH_2)_{q'}$ R^{70} R^{99} (II)

where q' is 0, 1, 2, 3 or 4;

s' is 0 or 1;

 X^{12} is C(O) or $S(O_2)$,

R⁷⁰ is hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkoxy, amino, N-C₁₋₆alkylamino, N,N-(C₁₋₆alkyl)₂amino, hydroxyC₂₋₆alkoxy, C₁₋₆alkoxyC₂₋₆alkoxy, aminoC₂₋₆alkoxy, N-C₁₋₆alkylaminoC₂₋₆alkoxy, N,N-(C₁₋₆alkyl)₂aminoC₂₋₆alkoxy or C₃₋₇cycloalkyl,

or R⁷⁰ is of the Formula (III):

wherein J is aryl, heteroaryl or heterocyclyl and K is a bond, oxy, imino, N-(C_{1-6} alkyl)imino, oxy C_{1-6} alkylene, imino C_{1-6} alkylene, N-(C_{1-6} alkyl)imino C_{1-6} alkylene, -NHC(O) -, -SO₂NH-, -NHSO₂- or -NHC(O)- C_{1-6} alkylene-,

and any aryl, heteroaryl or heterocyclyl group in a R⁷⁰ group may be optionally substituted by one or more groups selected from hydroxy, oxo, halo, trifluoromethyl, cyano, mercapto, nitro, amino, carboxy, carbamoyl, formyl, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -O-(C₁₋₃alkyl)-O-, C₁₋₆alkylS(O)_n- (wherein n is 0-2), N-C₁₋₆alkylamino, N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkoxycarbonyl, N-C₁₋₆alkylcarbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, C₂₋₆alkanoyl, C₁₋₆alkanoyloxy, C₁₋₆alkanoylamino, N-C₁₋₆alkylsulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino and C₁₋₆alkylsulphonyl-N-(C₁₋₆alkyl)amino,

or any aryl, heteroaryl or heterocyclyl group in a R⁷⁰ group may be optionally substituted with one or more groups of the Formula (IV):

 $-B^{\perp}(CH_2)_{p}-A^{1} \qquad (IV)$

wherein A^1 is halo, hydroxy, C_{1-6} alkoxy, cyano, amino, $N-C_{1-6}$ alkylamino, $N,N-(C_{1-6}$ alkyl)₂amino, carboxy, C_{1-6} alkoxycarbonyl, carbamoyl, $N-C_{1-6}$ alkylcarbamoyl or $N,N-(C_{1-6}$ alkyl)₂carbamoyl, p is 1 - 6, and B^1 is a bond, oxy, imino, $N-(C_{1-6}$ alkyl)imino or -NHC(O)-, with the proviso that p is 2 or more unless B^1 is a bond or -NHC(O)-;

or any aryl, heteroaryl or heterocyclyl group in a R⁷⁰ group may be optionally substituted with one or more groups of the Formula (V):

$$-E_{\overline{1}}D_{1}$$
 (A)

wherein D¹ is aryl, heteroaryl or heterocyclyl and E¹ is a bond, C₁₋₆alkylene, oxyC₁₋₆alkylene, oxy, imino, N-(C₁₋₆alkyl)imino, iminoC₁₋₆alkylene, N-(C₁₋₆alkylene, C₁₋₆alkylene, C₁₋₆alkylene, C₁₋₆alkylene, C₁₋₆alkylene, C₁₋₆alkylene, C₁₋₆alkylene-N-(C₁₋₆alkyl)-iminoC₁₋₆alkylene, -NHC(O)-, -NHSO₂-, -SO₂NH- or -NHC(O)-C₁₋₆alkylene-, and any aryl, heteroaryl or heterocyclyl group in a substituent on R⁴ may be optionally substituted with one or more groups selected from hydroxy, halo, C₁₋₆alkyl, C₁₋₆alkoxy, carboxy, C₁₋₆alkoxycarbonyl, carbamoyl, N-C₁₋₆alkylcarbamoyl, N-(C₁₋₆alkyl)₂carbamoyl, C₂₋₆alkanoyl, amino, N-C₁₋₆alkylamino and N,N-(C₁₋₆alkyl)₂amino,

and any C₃₋₇cycloalkyl or heterocyclyl group in a R⁷⁰ group may be optionally substituted with one or two oxo or thioxo substituents,

and any of the R⁷⁰ groups defined hereinbefore which comprises a CH₂ group which is attached to 2 carbon atoms or a CH₃ group which is attached to a carbon atom may optionally bear on each said CH₂ or CH₃ group a substituent selected from hydroxy, amino, C₁₋₆alkoxy, N-C₁₋₆alkylamino, N,N-(C₁₋₆alkyl)₂amino and heterocyclyl;

or R⁷⁰ may be cycloalkenyl or cycloalkynyl such as cyclohexenyl, or alkenyl optionally substituted by aryl;

and R^{99} is hydrogen or a group $C(O)R^{70}$ where R^{70} is as defined above;

3) a group of sub-formula (d) or (e)

$$-X^{10}(CH_2)_{p}-X^{11}R^{100}$$
 (d)

$$-X^{13}R^{100}$$
 (e)

where p' is 1-3, X^{10} and X^{11} are independently selected from a bond, -O-, -S- or NR^{101} - where R^{101} is hydrogen or a $C_{1.3}$ alkyl, provided that one of X^{10} or X^{11} is a bond; X^{13} is -O-, -S- or NR^{102} - where R^{102} is hydrogen or a $C_{1.3}$ alkyl and R^{100} is hydrogen or optionally substituted hydrocarbyl or optionally substituted heterocycyl, wherein any optional substituents may be functional groups as defined in claim 2 or claim 3; or

4) a group of formula (VI)

where R⁷¹ and R⁷² are independently selected from hydrogen or C₁₋₄alkyl, or R⁷¹ and R⁷² together form a bond, and R⁷³ is a group OR⁷⁴, NR⁷⁵R⁷⁶ where R⁷⁴, R⁷⁵ and R⁷⁶ are independently selected from optionally substituted hydrocarbyl or optionally substituted heterocyclic groups, and R⁷⁵ and R⁷⁶ may additionally form together with the nitrogen atom to which they are attached, an aromatic or non-aromatic heterocyclic ring which may contain further heteroatoms, wherein suitable optional substituents for hydrocarbyl or heterocyclic groups R⁷⁴, R⁷⁵ and R⁷⁶ include functional groups as defined in claim 2 or claim 3 and heterocyclic groups R⁷⁴, R⁷⁵ and R⁷⁶ may further be substituted by a hydrocarbyl group; 5) a group of sub-formula (f)

where p" is 0 or 1 and R⁸³ and R⁸⁴ are independently selected from hydrogen, optionally substituted hydrocarbyl or optionally substituted heterocyclyl, or R⁸³ and R⁸⁴ together with the nitrogen atom to which they are attached form an

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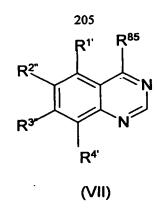
optionally substituted heterocyclic ring and where optional substituents hydrocarbyl or heterocyclic groups R⁸³ and R⁸⁴ include functional groups as defined in claim 2 or claim 3 and heterocyclic groups R⁸³ or R⁸⁴ may further be substituted by a hydrocarbyl group.

21. A compound according to claim 20 wherein R⁵ is substituted by a group of sub formula (II) which is a compound of formula (IIA)

$$(CH_2)_s$$
 $(CH_2)_{q'}$ R^{70} (IIA)

where s', q' and R⁷⁰ are as defined in claim 20.

- 22. A compound according to claim 20 or claim 21 wherein the substituent includes a group R⁷⁰ and said group is phenyl optionally substituted by halo.
- 23. A compound according to claim 20 where R⁵ is substituted by a group of formula (d) or (e) and R¹⁰⁰ is a group R⁷⁰ selected from optionally substituted phenyl or optionally substituted pyridyl.
- 24. A compound according to claim 20 or claim 23 wherein R⁵ is substituted by a group of sub-formula (d)
- 25. A compound according to any one of the preceding claim which is a phosphate prodrug of a compound of formula (I).
- 26. A method for preparing a compound of formula (I) as defined in claim 1, which method comprises reacting a compound of formula (VII)



where R¹', R²", R³", and R⁴' are equivalent to a group R¹, R², R³ and R⁴ as defined in relation to formula (I) or a precursor thereof, and R⁸⁵ is a leaving group, with a compound of formula (VIII)

$$H-X-R^5$$
 (VIII)

where X and R⁵ are as defined in relation to formula (I): and thereafter if desired or necessary converting a group R¹, R², R³ or R⁴ to a group R¹, R², R³ and R⁴ respectively or to a different such group.

- 27. A method for inhibiting aurora 2 kinase in a warm blooded animal, such as man, in need of such treatment, which comprises administering to said animal an effective amount of a compound according to claim 1, or salt, ester amide or prodrug thereof.
- 28. The use of a compound according to any one of claims 1 to 25 or salt, ester, amide or prodrug thereof, in the preparation of a medicament to inhibiting aurora 2 kinase.
- 29. A pharmaceutical composition comprising a compound according to any one of claims 1 to 25 or salt, ester amide or prodrug thereof, in combination with a pharmaceutically acceptable carrier.
- 30. A compound according to any one of claims 1 to 25 or salt, ester, amide or prodrug thereof for use in therapy.